

10/511108

In the Claims

DT04 Rec'd PCT/PTO 08 OCT 2004

1. (Currently Amended) A method for ~~discrimination of~~ discriminating p16^{INK4a} overexpressing metaplasias from p16^{INK4a} overexpressing neoplastic or preneoplastic lesions in a biological samples sample in the course of cytological testing procedures comprising:
 - a. determining the presence or absence of cells overexpression of p16^{INK4a} in said biological sample;
 - b. determining the presence or absence of cells expressing at least one high risk HPV ~~gene product~~ gene-product in said biological sample; and
 - c. assessing simultaneous presence of cells expressing high risk HPV gene-products with cells overexpressing p16^{INK4a} or the presence of cells overexpressing p16^{INK4a} alone;
 - d. wherein the simultaneous presence of cells expressing high risk HPV gene-products with cells overexpressing p16^{INK4a} is indicative for neoplastic or preneoplastic lesion.
2. (Currently Amended) A The method according to claim 1, wherein the high risk HPV gene-products are predominately expressed in early neoplastic and/or preneoplastic lesions.
3. (Currently Amended) A The method according to ~~any one of the preceding claims~~ claim 1, wherein at least one of the HPV gene-products is encoded by the HPV E7 gene.
4. (Currently Amended) A The method according to claim 1, wherein at least one of the HPV gene-products is encoded by HPV E2 and/or E6 genes.
5. (Currently Amended) A The method according to claim 1, wherein at least one of the HPV gene-products is encoded by HPV L1 and/or L2 genes.
6. (Currently Amended) A The method according to ~~any one of the preceding claims~~ claim 1, wherein the HPV ~~gene product~~ gene-product is a polypeptide or an RNA molecule.

7. (Currently Amended) The method according to ~~any one of the preceding claims~~ claim 1, wherein the neoplastic or preneoplastic lesions are lesions of the anogenital tract.
8. (Currently Amended) The method according to claim 7, wherein the lesion of the anogenital tract is a lesion of the uterine cervix.
9. (Currently Amended) A The method according to ~~any preceding claim~~ claim 1, wherein the biological sample is a sample containing cells of anogenital origin.
10. (Currently Amended) A The method according to claim 9, wherein the cells of anogenital origin are cells originating from the uterine cervix.
11. (Currently Amended) A The method according to claim 10, wherein the biological sample is a Pap-smear or a cytological preparation of the cervix uteri.
12. (Currently Amended) A The method according to ~~any one of the preceding claims~~ claim 1, wherein the detection of the HPV gene-products and of the p16^{INK4a} ~~molecules~~ is performed using ~~at least one probe specifically~~ one or more probes specific for ~~the molecules to be detected~~ the HPV gene-products and p16^{INK4a}.
13. (Currently Amended) A The method according to claim 12, wherein the probe is detectably labelled.
14. (Currently Amended) A The method according to claim 13, wherein the label is selected from the group consisting of a radioisotope, a bioluminescent compound, a chemiluminescent compound, a fluorescent compound, a metal chelate, or an enzyme.
15. (Currently Amended) A The method according to ~~any one of the claims 12 to 14~~ claim 12, wherein the probe is a protein polypeptide and/or a nucleic acid.
16. (Currently Amended) A The method according to claim 15, wherein ~~at least one~~ the probe is an antibody directed against a high risk HPV encoded ~~gene product~~ gene-product or p16^{INK4a}.
17. (Original) The method according to claim 16, which comprises an immuno-cytochemical staining procedure.

18. (Currently Amended) The method according to claim 15, wherein ~~at least one~~ the probe is a nucleic acid specifically hybridizing to a high risk HPV ~~gene-product~~ gene-product.
19. (Original) The method according to claim 18, which comprises an in situ hybridization reaction.
20. (Original) The method according to claim 18, which comprises a nucleic acid amplification reaction.
21. (Original) The method according to claim 20, wherein the nucleic acid amplification reaction is PCR or LCR.
22. (Currently Amended) ~~A~~ The method according to ~~any of the preceding claims~~ Claim 15, wherein detection ~~reactions of the HPV gene-products and~~ p16^{INK4a} is carried out using nucleic acid probes and polypeptide probes ~~are carried out~~ simultaneously.
23. (Currently Amended) ~~A~~ The method according to ~~any one of the preceding claims~~ claim 1, wherein the high risk HPV gene-products are gene-products of the cancer associated HPV subtypes HPV 16, 18, 31, 33, 35, 39, 45, 51, 52, 56 ~~and or~~ or 58.
24. (Currently Amended) ~~A~~ The method according to ~~any of the preceding claims~~ claim 1, wherein overexpression of p16^{INK4a} simultaneous to expression of at least one high risk HPV ~~gene-product~~ gene-products in at least one single cell is determined.
25. (Currently Amended) ~~A kit for performing the method according to any one of the preceding claims, which is a diagnostic kit or a~~ or research kit, comprising
- a. probes for the detection of the presence or absence of the overexpression of p16^{INK4a} in biological samples, and
 - b. one or more probes for the detection of the presence or absence of the expression of one or more HPV gene-products in biological samples.
26. (Currently Amended) ~~A~~ The kit according to claim 25 furthermore comprising
- a. a p16^{INK4a} sample for carrying out a positive control reaction, and
 - b. one or more samples of HPV gene-products for carrying out positive control reactions.